

The University of Chicago

THE ELECTROSTATIC
INFLUENCE OF SUBSTITUENTS
ON DISSOCIATION CONSTANTS
AND REACTION VELOCITY

A DISSERTATION SUBMITTED TO THE
FACULTY OF THE DIVISION OF THE
PHYSICAL SCIENCES IN CANDIDACY
FOR THE DEGREE OF DOCTOR OF
PHILOSOPHY

DEPARTMENT OF CHEMISTRY

1939

By
MARTIN W. SHOOKHOFF

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The Electrostatic Influence of Substituents on the Dissociation Constants of Organic Acids.

By MARTIN W. SHOOKHOFF

Bjerrum originated the hypothesis that the ratio of the ionization constant of an acid with a polar substituent to that of the corresponding unsubstituted acid depends upon a statistical factor and upon the electrostatic influence of the substituent.¹ While his computation of the magnitude of the electrostatic effect can be regarded only as a first approximation, the theory formed the basis of a new mathematical treatment by Kirkwood and Westheimer.² This development departs from Bjerrum's treatment in the assumption that the molecules are cavities of low dielectric constant in which the charges are imbedded. The equations derived are of the same form as Bjerrum's, but D , the dielectric constant of the solvent, is replaced by D_E , the "effective" dielectric constant, a function of the shape of the molecule, the position of the charges within the molecule, the dielectric constant of the solvent, and the dielectric constant of the cavity. The equation for a symmetrical dibasic acid is

$$\log K_1/\sigma K_2 = \frac{e^2}{2.303kTRD_E}$$

K_1 and K_2 are the first and second dissociation constants of the acid, e the electronic charge, k the Boltzmann constant, T the absolute temperature, and R the interprotonic distance. σ , the statistical factor, in this instance is equal to four. The equation for a dipole substituted acid is

$$\log K_1/\sigma K_2 = \frac{eM \cos \zeta}{2.303kTR^2D_E}$$

K_1 is the ionization constant of the dipole substituted acid, K_2 that of the corresponding unsubstituted acid, M the dipole moment of the substituent, ζ the angle between the dipole and the line joining its center with the ionizable proton, and R is the distance between the center of the dipole and the proton. D_E has been calculated for molecules which approximate in shape either a sphere, or a prolate ellipsoid of revolution in which the proton and the substituent are at the foci.² In the former case, D_E is calculated as a function of the position of the charges in the

molecule, in the latter as a function of the eccentricity of the ellipsoid.

Several illustrating examples showed that the interprotonic distances in dicarboxylic acids calculated on this basis are consistent with distances estimated from independent considerations, even for those cases for which the simple Bjerrum theory is inadequate. Further, in contrast with the simple theory³ reasonable values of the proton dipole distance were obtained for a few dipole substituted acids.

The present paper will give the interprotonic or proton-dipole separation, calculated by the new theory, for a large number of organic acids. For comparison, the distance calculated on the basis of an extended chain model will again be taken as an upper limit, the distance calculated on the basis of free rotation as a reasonable but not a rigid lower limit. It will be shown that this new development of Bjerrum's hypothesis accounts satisfactorily for the ratio of the dissociation constants of aliphatic dibasic acids, for the ratio of the dissociation constants of dipole substituted aliphatic acids to those of unsubstituted acids, for the ratio of the dissociation constants of the salts of the esters of amino acids to those of the corresponding amino acids, for the effect of alkyl groups and of solvent upon the dissociation constant ratio.

In Table I are assembled the data for the symmetrical dibasic saturated aliphatic acids. In column 1 the name of the acid is given with a key to the authority for the dissociation constant data, in column 2, ΔpK , defined by the relationship $\Delta pK = \log K_1/\sigma K_2$ where K_1 and K_2 are the first and second dissociation constants of the dibasic acid, and σ is the statistical factor. In the column marked R , the interprotonic distance in Å. computed from ionization constant data by means of the new formulation, is given to the nearest 0.05 Å. $R_{\max}$ is the maximum interprotonic distance in Å. on the basis of accepted valence angles and bond lengths, placing the protons conventionally 1.45 Å. beyond the terminal carbon atom and on the extension of the last carbon to

(1) Bjerrum, *Z. physik. Chem.*, **106**, 219 (1923).

(2) Kirkwood and Westheimer, *J. Chem. Phys.*, **6**, 506 (1938); Westheimer and Kirkwood, *ibid.*, **6**, 513 (1938).

(3) Eucken, *Z. angew. Chem.*, **45**, 203 (1932).

TABLE I
 DIBASIC ALIPHATIC ACIDS

Acid	ΔpK	$\cos \vartheta$	R	Length in Å.		R_B
				$R_{Max.}$	R_F	
Oxalic acid ^a	2.36	-1.00	3.85	4.44	3.50	0.91
Malonic acid ^a	2.26	-1.00	4.10	4.87	4.12	1.36
Methylmalonic acid ^a	1.89	-0.33	4.05	4.87	4.12	1.62
Ethylmalonic acid ^a	2.05	- .33	4.10	4.87	4.12	1.50
Dimethylmalonic acid ^a	2.29	- .33	4.15	4.87	4.12	1.34
Diethylmalonic acid ^a	4.48		3.75	4.87	4.12	0.69
Methylethylmalonic acid ^a	2.95	- .33	4.10	4.87	4.12	1.04
Succinic acid ^b	0.84		5.75	6.66	4.66	3.65
α, α' -Dimethylsuccinic acid (209°) ^a	1.56		5.35	6.66	4.66	1.97
α, α' -Dimethylsuccinic acid (129°) ^a	1.66		5.30	6.66	4.66	1.85
α, α' -Diethylsuccinic acid (192°) ^a	2.23	-1.00	5.10	6.66	4.66	1.37
α, α' -Diethylsuccinic acid (129°) ^a	2.49	-1.00	5.00	6.66	4.66	1.23
Tetramethylsuccinic acid ^a	4.19	-1.00	4.80	6.66	4.66	0.74
<i>dl</i> -Tartaric acid ^a	0.75		6.00	6.66	4.66	4.09
<i>meso</i> -Tartaric acid ^a	.99		5.50	6.66	4.66	3.10
Glutaric acid ^b	.47		7.00	7.59	5.15	6.53
β -Methylglutaric acid ^b	.56		6.85	7.59	5.15	5.48
β -Ethylglutaric acid ^c	.44		7.60	7.59	5.15	7.05
β -Propylglutaric acid ^c	.47		7.75	7.59	5.15	6.89
β, β -Dimethylglutaric acid ^b	1.97		5.25	7.59	5.15	1.56
β, β -Diethylglutaric acid ^d	3.66	-1.00	4.70	7.59	5.15	0.84
β, β -Dipropylglutaric acid ^a	3.02	-1.00	5.15	7.59	5.15	1.03
β, β -Methylethylglutaric acid ^a	2.48		5.10	7.59	5.15	1.24
Adipic acid ^b	0.38		7.75	9.02	5.59	8.11
Pimelic acid ^d	.34		8.30	9.91	6.00	9.12
Suberic acid ^a	.28		9.30	11.46	6.38	10.9
Azelaic acid ^a	.26		9.85	12.42	6.74	11.9
<i>cis</i> -Caronic acid ^{b, e}	5.36	+0.15	3.30	4.26	4.08	0.58
<i>trans</i> -Caronic acid ^{b, e}	0.90	- .73	5.45	6.65	5.52	3.44
Cyclopropane- <i>cis</i> -dicarboxylic acid ^{a, e}	2.54	+ .16	3.40	4.26	4.08	1.22
Cyclopropane- <i>trans</i> -dicarboxylic acid ^{a, e}	0.87	- .72	5.00	6.65	5.52	3.56

^a Landolt-Börnstein, "Physikalisch-chemische Tabellen," Erg. III c. ^b Jones and Soper, *J. Chem. Soc.*, 133 (1936).

^c Ingold and Mohrrehn, *ibid.*, 951 (1935), correction. ^d Landolt-Börnstein, "Physikalisch-chemische Tabellen," Erg. II b. ^e The protonic separation on the basis of free rotation for the caronic and cyclopropane-dicarboxylic acids was computed according to an equation kindly supplied to the author by Professor J. G. Kirkwood. The ring was assumed rigid, and the extracyclic valence angle set equal to the angle between each gem substituent and the adjacent ring bond. In these cases $\cos \vartheta$ and R were determined by the method of successive approximations; elsewhere $\cos \vartheta$ refers to the extended model. ^f The length of the carbon-oxygen bond in the carboxyl group was chosen as 1.29 Å.; otherwise the accepted bond lengths were used. The tetrahedral angle was used throughout except that the angle between the terminal carbon to carbon bond and the carbon to oxygen bond of the carboxyl group was taken as 120°, and the angle between the carbon to oxygen and the oxygen to hydrogen bonds was taken as 90°.

carbon bond. R_F is the root mean square separation of the protons calculated on the basis of free rotation according to Eyring.⁴ Finally, R_B refers to the distance obtained from Bjerrum's formula. In those cases treated on the basis of an ellipsoidal model, the protons were placed at the foci. However, when a spherical model was employed, it was necessary to choose a center for the molecule. In some instances, as with dimethylmalonic acid, the location of the center is quite obvious. In others, however, such as malonic acid itself, or its diethyl derivative, it is

more difficult to choose a center without ambiguity. In these latter cases, it was customary to make the computation with two or more different values of ϑ , the angle made by the lines joining the two protons with the center. While the value of $\cos \vartheta$ is given appropriate to the interprotonic distance quoted, in some cases variation of ϑ between reasonable limits caused an uncertainty in R as great as 0.3 Å. Likewise, in those cases in which the shape of the molecule is intermediate between a sphere and a prolate ellipsoid, a computation on the basis of both possibilities revealed uncertainties in the value of R of the same order of magnitude. Where no value of $\cos \vartheta$ is given

(4) Eyring, *Phys. Rev.*, **39**, 746 (1932). It is worth pointing out that, for Eyring's formula to be valid, free rotation is not actually necessary. See ref. 2, p. 510, footnote 8.

in Table I, the computation was made on the basis of an ellipsoidal model.

On inspection, Table I reveals that in all cases the new formulation gives a reasonable value for the interprotonic distance. Bjerrum's equation, while equally effective for glutaric acid and its normal higher homologs, gives distances which are almost certainly too short for its lower homologs and for polymethylated acids.

Of especial interest is the comparison of the lengths of the methylated with those of the unsubstituted acids. In the case of the malonic acids, for example, the interprotonic distance computed by the Bjerrum equation varies from 0.69 Å. for diethylmalonic acid to 1.62 Å. for the methyl substituted compound. Not only is the magnitude of separation small, but the large variation in distance with a slight structural change is unlikely. On the basis of the new formulation, the separation varies from 3.75 to 4.15 Å., lengths all of which are quite close to the interprotonic distance computed for free rotation. In view of the approximate constancy of the interprotonic distance, it may prove necessary to reexamine the part of the evidence for Ingold's theory of the deflection of the valence angles in alkylated acids which received its support from a consideration of dissociation constant data.⁵ Since the present formulation shows quite clearly that the variation of interprotonic distance with substitution is a phenomenon of the second order in magnitude, it is interesting to account qualitatively for the approximate constancy of R despite the large variation of ΔpK . The new equations predict, to be sure, a smaller change of R with variation in ΔpK than does Bjerrum's. But a second effect is also noticeable. The more alkyl substituents in the acid, the larger is the cavity in the solvent. This lowers the effective dielectric constant and hence magnifies the electrostatic effect of the negative charge of the acid-ion on the ionization of the second proton. In this connection it is possible to discuss the first and second dissociation constants separately. In a later section of this paper it is shown that, at least as a first approximation, the fact that the first dissociation constant of malonic acid is greater than the dissociation constant of propionic acid can be explained on the basis of a statistical factor of two and the electrostatic effect of one carboxyl dipole

on the dissociation of a proton from the other carboxyl group. It is noteworthy that the first ionization constant of diethylmalonic acid is greater than the first ionization constant of malonic acid, while the second ionization constant of the substituted acid is decidedly less than that of the unsubstituted acid. The reason is at once clear why the ethyl groups increase one ionization constant but decrease the other. In each case the alkyl groups have little direct influence, but, by lowering the effective dielectric constant, they increase the electrostatic potential of the charges already present. It is noteworthy that variation in the angle between the lines joining the protons with the center of the sphere also changes the effective dielectric constant.

In Table II the data for the amino acids are presented. A direct computation of the protonic separation in a glycine salt, for example, would result from a comparison of the ionization constants of the ammonium groups regarded as acids in the Brönsted sense, in $^+\text{NH}_3\text{CH}_2\text{COO}^-$ and in $^+\text{NH}_3\text{CH}_2\text{COOH}$. According to the zwitterion hypothesis, the ionization constant of the ammonium group of the latter cannot be measured, but it is probable that it will not differ greatly from the dissociation constant of the ester-salt, $^+\text{NH}_3\text{CH}_2\text{COOCH}_3$.⁶ On the basis of this approximation, Neuberger⁷ applied the simple Bjerrum theory to the amino acids. The data presented here show again that the simple Bjerrum theory is only approximate for the smaller molecules, while the present theory adequately accounts for the ratio of the ionization constant of the ester salt to that of the amino acid.

In the column of Table II marked R_C are given the distances between the positive and negative charges in the neutral amino acids, as estimated by Cohn and his co-workers⁸ from dielectric constant measurements. While these lengths should be somewhat less than the interprotonic distances, they are of especial interest because they are experimental values. A comparison of R with them is independent of the uncertainties relative to the extent of hindered rotation which affect the comparison of R with the separation computed on the basis of free rotation or an extended chain model.

(6) See Wegscheider, *Monatsh.*, **16**, 153 (1895), for a comparison of the effect of carbethoxy and carboxyl groups upon the dissociation constants of acids.

(7) Neuberger, *Proc. Roy. Soc. (London)*, **A158**, 68 (1937).

(8) Cohn, *Ann. Rev. Biochem.*, **4**, 93 (1935).

(5) Ingold, *et al.*, *J. Chem. Soc.*, 1318, 1594, 2267 (1928); 1691 (1929); 2153 (1931); 949 (1935).

TABLE II
AMINO ACIDS

Amino acid	ΔpK^b	$\cos \theta$	R	R_{Max}	Length in Å. R_F^c	R_C	R_B
Glycine ^a	2.02	-1.00	4.05	3.97	3.56	3.17	1.53
Alanine ^a	2.07	-0.33	3.85	3.97	3.56	3.17	1.50
β -Alanine ^a	1.06		5.15	5.49	4.19	3.97	2.92
γ -Aminobutyric acid ^a	0.72		6.10	6.46	4.72	4.75	4.31
δ -Aminovaleric acid ^a	.62		6.55	7.90	5.19	5.23	5.00
ϵ -Aminocaproic acid ^a	.38		7.85	8.97	5.63	5.76	8.16
Glycylglycine ^a	.56		6.50	7.65	5.17	5.51	5.54

^a Neuberger, *Proc. Roy. Soc. (London)*, **A158**, 68 (1937). ^b ΔpK is defined as $\log_{10} K_E/K_Z$, where K_E is the ionization constant of the ester salt, K_Z of the free amino acid, each regarded as an acid according to the Brönsted definition. ^c The average position of the hydrogen atoms attached to nitrogen was chosen as 0.33 Å. beyond the nitrogen atom in the direction of the carbon to nitrogen bond. In glycylglycine, the angle between the amide linkage and the adjacent carbon to carbon bond was chosen as 120°.

TABLE III
SUBSTITUTED MONOBASIC ACIDS

Acid	pK	Eq.	$\cos \zeta$	R	$R_{\text{Max.}}$	R_F	$R_{\text{Min.}}$	R_B
Fluoroacetic acid ^{a,b}	2.09	<i>S</i>	0.55	2.80	3.29	2.91	1.85	0.49
Chloroacetic acid ^{a,c}	1.89	<i>S</i>	.58	3.00	3.39	2.99	1.84	.55
Bromoacetic acid ^{a,c}	1.87	<i>S</i>	.60	3.05	3.43	3.05	1.82	.54
Iodoacetic acid ^{a,c}	1.59	<i>S</i>	.62	3.10	3.49	3.09	1.81	.55
Glycolic acid ^{a,c}	0.93	<i>E</i>	.36	3.10	3.72	3.33	1.86	.61
Cyanoacetic acid ^a	2.30	<i>E</i>	.78	3.80	4.21	3.81	2.11	.86
β -Chloropropionic acid ^{a,c}	0.85	<i>E</i>	.94	4.25	4.61	3.69	1.27	1.06
β -Bromopropionic acid ^{a,c}	.88	<i>E</i>	.94	4.30	4.69	3.73	1.22	1.02
β -Iodopropionic acid ^{a,c}	.79	<i>E</i>	.94	5.20	4.78	3.78	1.18	1.01
γ -Chlorobutyric acid ^{a,d}	.30	<i>E</i>	.71	5.40	5.80	4.29		1.52
γ -Bromobutyric acid ^{a,d}	.23	<i>E</i>	.70	4.40	5.86	4.33		1.70

^a Landolt-Börnstein, "Physikalisch-chemische Tabellen," Erg. III c. ^b Swarts, *Bull. sci. acad. roy. Belg.*, [5] **8**, 343 (1922). ^c Larsson, *Z. physik. Chem.*, **165A**, 53 (1933). ^d Landolt-Börnstein, "Physikalisch-chemische Tabellen," Hauptwerke. ^e The average value of $\cos \zeta$ is given.

The fact that reasonable values of R can be obtained completes that argument in favor of the zwitterion hypothesis which is founded upon the comparison of ionization constants.

In Table III the available data for the dipole substituted aliphatic acids are summarized. Here the dissociation constant of each substituted acid is compared with that of the corresponding unsubstituted acid; the statistical factor is, of course, unity. Rather than the dipole moments of the substituent groups, used in the previous publications, the difference between a carbon-hydrogen moment and the moment of the substituent group is desired. Since the resultant moment of the three carbon-hydrogen bonds in a monosubstituted methane is approximately equal to that of one carbon-hydrogen bond directly opposed to the substituent, the dipole moments, determined in the gas phase, of the substituted methanes were used in the computations quoted in Table III.⁹ The letter *S* in column three refers to the fact that the computations were

made with a spherical model, placing the center of the dipole and the ionizable proton on a diameter; the letter *E* refers to the fact that an ellipsoidal model was used, and that the center of the dipole and the ionizable proton were placed at the foci. ζ is the angle the dipole makes with the line joining its center to the proton. When the dipole group is not linear (as in the case of the hydroxyl group), the average value of $\cos \zeta$ was employed, assuming free rotation of the dipolar group. In each case, the proton was conventionally placed on the extension of the last carbon to carbon bond and beyond the terminal carbon atom, and $\cos \zeta$ determined by the method of successive approximations. The values of $\cos \zeta$ found in this manner always closely approximated that in the fully extended acid.

For the computation of R_B , the separation of proton and dipole according to the Bjerrum-Eucken hypothesis, $\cos \zeta$ was assumed equal to that in the fully extended model. Even when $\cos \zeta$ is assigned the maximum possible value of unity, the simple theory often leads to values of

(9) Smyth, *J. Phys. Chem.*, **41**, 209 (1937).

R_B less than the minimum separation (R_{Min} in Table III) possible without distortion of valence bonds or angles. Under these circumstances, the method of successive approximations is no longer sensible.

While the simple Bjerrum-Eucken equation is inadequate, the reasonable values of the proton-dipole separation obtained from the new formulation provide a broad justification for Bjerrum's hypothesis.

Among the dipolar substituents which increase the strength of an acid is the carboxyl group. The first dissociation constant of succinic acid, for example, is considerably greater than the dissociation constant of butyric acid, even when the statistical factor of two for the dibasic acid is taken into account. The application of the present theory is made difficult, however, by the following considerations: while Zahn¹⁰ has determined the dipole moment of the carboxyl group in monomeric aliphatic acids, the angle between the dipole and the terminal carbon to carbon bond is unknown. It can be estimated, using Williams' formula¹¹ and the dipole moments of the methyl esters of terephthalic acid and of diphenyl *p,p'*-dicarboxylic acid,¹² that the ester group exerts a moment which is approximately at an angle of 60° with the last carbon to carbon bond. The recent work of Marsden and Sutton¹³ is roughly in accord with this estimate. While the angle of the carboxyl moment is not known, it is a reasonable assumption, in the absence of further information, that the carboxyl group is at least no less symmetrical than the carbomethoxy group.

Besides the uncertainty in the angle of the carboxyl dipole, an additional complication arises from the fact that the moment is a composite one. The charge distribution is such that the carboxyl group will be more effective in increasing the strength of an acid than could be predicted from the resultant moment.

The data of Table IV were calculated using the following assumptions. The moment of the carboxyl group was chosen as 1.7 Debye units, and was placed in the center of the carboxyl group, at an angle of 60° with the terminal carbon to carbon bond. In addition to R_{Max} and R_F , the protonic separation R_D , determined from the first and second dissociation constants of the

dibasic acid and recorded in Table I, is included as a standard of reference. Since the carboxyl dipole is located somewhere near the center of the carboxyl group, R_D should exceed R by about 0.7 Å. The fact that the actual difference between R_D and R is greater than 0.7 Å. is in qualitative agreement with the deviations anticipated because of the composite nature of the carboxyl moment and the uncertainty relative to its angle.

TABLE IV
DIBASIC ALIPHATIC ACIDS REGARDED AS CARBOXYL SUBSTITUTED MONOBASIC ACIDS

Acid	ΔpK	Eq.	Average Cos ζ	R	R_{Max}	R_F	R_D	R_B
Oxalic acid ^a	3.22	S	0.50	2.3	3.71	3.24	3.85	0.4
Malonic acid ^a	1.75	S	.38	2.6	4.30	3.91	4.10	.4
Succinic acid ^{a,b}	0.36	E	.49	4.6	5.94	4.48	5.75	1.2
Glutaric acid ^{a,b}	.18	E	.39	5.1	6.81	4.98	7.00	1.5

^a Landolt-Börnstein, "Physikalisch-chemische Tabellen," Erg. III c. ^b Jones and Soper, *J. Chem. Soc.*, 133 (1936).

Finally, the effect of change of solvent upon ΔpK is of interest. There are very few data available relating to the dissociation constants of saturated aliphatic carboxylic acids in pure solvents other than water. This much, however, can be noted. In the Bjerrum expression for ΔpK , the dielectric constant of the medium enters in the denominator to the first power. It would then be anticipated that the logarithm of the ratio of the dissociation constant of chloroacetic acid to that of acetic acid would be from two and a half to three times as great in methyl or ethyl alcohol as in water. The data are available for the chloroacetic acid-acetic acid pair and for the glycolic acid-acetic acid pair in various alcohol-water mixtures.¹⁴ Since ΔpK remains essentially constant throughout, it is probably safe to extrapolate, and estimate that the ratio of the dissociation constants will be the same in pure alcohol as in water. As a matter of fact, the *H* function of Hammett and Deyrup¹⁵ is based on the assumption, experimentally justifiable for carboxylic acids, that the ratio of the dissociation constants of two acids of the same charge type is little affected by change of solvent. This statement, directly opposed to the predictions of the simple Bjerrum-Eucken equations, is in conformity with the present theory. The effective dielectric constant in the case of chloroacetic and

(10) Zahn, *Phys. Rev.*, **37**, 1516 (1931).

(11) Williams, *Z. physik. Chem.*, **138A**, 75 (1928).

(12) See Sidgwick, *Trans. Faraday Soc.*, **30**, 904 (1934).

(13) Marsden and Sutton, *J. Chem. Soc.*, 1383 (1936).

(14) Michaelis and Mizutani, *Z. physik. Chem.*, **116**, 135 (1925); Mizutani, *ibid.*, **118**, 318 (1925).

(15) Hammett and Deyrup, *J. Am. Chem. Soc.*, **54**, 2721 (1932); cf. Wynne-Jones, *Proc. Roy. Soc. (London)*, **A140**, 440 (1933).

glycolic acids is already low, and near the value of D_i , the internal dielectric constant. Computations of D_E for methanol and ethanol show that, for the case of the dipoles in chloroacetic and glycolic acids, using alcohol instead of water as solvent will not appreciably increase the electrostatic effect.

While it is not advisable to extrapolate the data for the aliphatic dicarboxylic acids¹⁴ obtained in water-alcohol mixtures to pure alcohol as solvent, it is obvious that the ratio of the first and second dissociation constants for malonic and succinic acids, while greater in methyl and ethyl alcohols than in water, is certainly not increased by as much as the simple theory predicts, but by a smaller amount, a fact at least qualitatively in agreement with the prediction of the present theory for these cases. Quantitative agreement, in the case of non-aqueous solutions, must await further experimentation.

The errors inherent in the present method of estimating the electrostatic effect, other than

those given here, have been discussed in the previous publications. The reasons for omitting consideration of Ingold's attempt to take electrostriction and electrical saturation into account¹⁶ have been presented elsewhere.² The molecular volumes necessary for the calculations have been estimated from Traube's rule.¹⁷

Summary

The new mathematical formulation, by Kirkwood and Westheimer, of the electrostatic effect of a substituent, has been shown to account satisfactorily for the ratio of the ionization constant of a dibasic acid, for the ratio of the ionization constant of a dipole substituted acid to that of the unsubstituted acid, for the ratio of the ionization constant of an amino acid with that of a salt of its ester. The theory also accounts for the effect of alkyl groups and, at least in the few cases which can now be examined, for the effect of solvent, upon the ionization constant ratio.

(16) Ingold, *J. Chem. Soc.*, 2179 (1931).

(17) Traube, *Saml. chem. chem.-tech. Vortr.*, 4, 255 (1899).

The Electrostatic Influence of Substituents on Reaction Rates.

BY MARTIN W. SHOOKHOFF

Ingold has postulated that the effect of a polar substituent on the rate of saponification of an aliphatic ester, like the effect of such a substituent on the ionization constant of an acid, is largely electrostatic. In 1930¹ he employed Bjerrum's quantitative electrostatic formulation² to compute, from the ratios of the rates of saponification of the first and second ester groups, the separation of the carbalkoxy groups in a series of esters of dibasic acids. Ingold's evidence went far toward establishing his hypothesis in those cases in which the molecule is long and the substituent can be regarded as a negative charge.

Kirkwood and Westheimer³ have recently refined Bjerrum's approximate computations of the electrostatic free energy involved in a chemical reaction; the success of the new equations, while general, has been most conspicuous in the considerations of the ionization constants of short dibasic and of dipole substituted acids,⁴ cases for which the older formulation is inadequate.

(1) Ingold, *J. Chem. Soc.*, 1375 (1930), 2170 (1931); Ingold and Mohrheun, *ibid.*, 1482 (1935).

(2) Bjerrum, *Z. physik. Chem.*, **106**, 219 (1923).

(3) Kirkwood and Westheimer, *J. Chem. Phys.*, **6**, 506 (1938); Westheimer and Kirkwood, *ibid.*, **6**, 513 (1938).

(4) Westheimer and Shookhoff, *J. Am. Chem. Soc.*, **61**, 555 (1939); Westheimer, *ibid.*, **61**, 1977 (1939); cf. Eucken, *Z. angew. Chem.*, **45**, 203 (1932).

The shortcomings of Ingold's modified equation⁵ have been presented previously.

The present paper deals with the rate of alkaline hydrolysis of esters and amides in cases in which the substituent is a negative charge, a positive charge and a dipole, all placed close to the seat of the reaction. When the substituent is close to the ester or amide bond that is broken, the rates of hydrolysis of the substituted and unsubstituted compounds differ by a factor of a hundred or more. Since the measurements were made by conductivity, very slow and very fast reactions were excluded: the former because of action of alkali on the glass of the cell, the latter because of the time required to attain thermal equilibrium. These considerations necessitated a careful selection of the pairs of compounds employed.

To illustrate the effect of a negative charge as substituent, the rate of alkaline hydrolysis of the sodium salt of oxamic acid was compared with the rate for oxamide; to illustrate the effect of a positive charge, the rate of saponification of the chloride of the tertiary butyl ester of betaine was compared with the rate for the tertiary butyl ester of dimethylglycine; and to illustrate the

(5) Ingold, *J. Chem. Soc.*, 2179 (1931).

effect of a dipole, the rate of saponification of the tertiary butyl ester of chloroacetic acid was compared with the rate for the tertiary butyl ester of acetic acid.

The equations of Kirkwood and Westheimer apply accurately only to spheres and to prolate ellipsoids in which substituents and charges are at the foci. Due to the experimental limitations mentioned above, some sacrifice in the shape of the molecule was unavoidable.

Theoretical

Ingold treated the reaction velocity problem by means of Christiansen's theory,⁶ that is, as a case in which the local concentration of hydroxide ions differs, due to the presence in the molecule of a polar substituent, from that in the remainder of the solution. The assumptions involved can be more conveniently stated, however, when the problem is formulated in Brönsted's terms.⁷

Brönsted postulated a rapid equilibrium between the reactants and an activated complex, followed by a slow decomposition of the activated complex to form the reaction products. In order to apply the electrostatic theory, it is further necessary to assume that the rates of decomposition will be the same for activated complexes formed from two closely similar molecules.⁸ Stated mathematically

$$k_{\text{obsd.}} = kK \text{ and } k'_{\text{obsd.}} = k'K'$$

$k_{\text{obsd.}}$ and $k'_{\text{obsd.}}$ are the observed velocity constants, corrected to infinite dilution, for the bimolecular reactions, and K and K' are the equilibrium constants for the formation of the two activated complexes. If k and k' , the rate constants for the decomposition of the activated complexes, are assumed equal, then

$$k_{\text{obsd.}}/k'_{\text{obsd.}} = K/K'$$

In other words, to compute the ratio of the velocity constants at infinite dilution, it is only necessary to compute the ratio of the equilibrium constants for the formation of the critical complexes.

The rest of the argument exactly parallels that given by Kirkwood and Westheimer³ for the case of the ionization constants of acids with and without polar substituents. $k''T \log_e K - k''T \log_e K'$ is equal to $\Delta w'$, where k'' is Boltz-

mann's constant, T the absolute temperature, and $\Delta w'$ is the average reversible work expended in the transfer of a hydroxide ion from the unsubstituted activated complex to the substituted ester, infinitely separated in the solvent. Part of $\Delta w'$ is an entropy term, arising from differences in molecular symmetry. The electrostatic part of $\Delta w'$, called Δw , is that which can be computed. The part of $\Delta w'$ connected with the intrinsic structure of the molecules is by no means to be overlooked, but it is assumed that, as a first approximation, it will vanish because of cancellations between the substituted and unsubstituted compounds.

It follows, therefore, that

$$\Delta w = k''T \log_e K/\sigma K' = k''T \log_e k/\sigma k' = 2.303 k''T \Delta \log k$$

where k'' is the Boltzmann constant, σ is a statistical factor (equal to two in the saponification of esters or amides of dibasic acids) and the equation serves to define $\Delta \log k$.

From the equations of Kirkwood and Westheimer and from the experimental values of $\Delta \log k$, it is possible to compute the distance between the negative charge in the activated complexes, and the positive charge in the chloride of tertiary butyl betaine, the center of the dipole in tertiary butyl chloroacetate, and a positive charge in oxamide, located approximately in the position of the ionizable proton in oxamic acid. These distances are then compared with those obtained from an independent source.

Experimental

Apparatus.—Conductivity was measured with a calibrated Leeds and Northrup bridge, using a slide wire of the Kohlrausch type, and a Clough-Brengle audio frequency oscillator as the source of current. The apparatus was slightly modified⁹ from the standard Washburn type, and was capable of measuring resistances with a precision of 0.01%.

The design of the conductivity cells was dictated primarily by the experimental observation that the percentage time rate of change of conductivity due to the solution of the glass in alkali increases with temperature, dilution, and the ratio of surface to volume, as shown in Table I. Cell A, used at alkali concentrations of 0.0003 to 0.003 was spherical, of one liter capacity, and had bright electrodes, 1.8 cm. in diameter and 2 cm. apart. Due to the large size of this cell, at least an hour was necessary to attain temperature equilibrium; it was not, then, very satisfactory for the more rapid reactions. For the concentration range 0.003 to 0.05, cell B was used. It was cylindrical in shape, 3 cm. in diameter and 11 cm.

(9) Jones and Josephs, *J. Am. Chem. Soc.*, **50**, 1049 (1928).

(6) Christiansen, *Z. physik. Chem.*, **113**, 35 (1924).

(7) Brönsted, *Chem. Rev.*, **5**, 231 (1928).

(8) The application of electrostatic theory to the problem of the change of rate with solvent involves a more limited assumption (Scatchard, *J. Chem. Phys.*, **7**, 657 (1939)). Since the transmission coefficient is usually in the neighborhood of unity, a broader assumption is involved in Eyring's theory (*ibid.*, **3**, 107 (1935)).

long, with lightly platinized electrodes 1 cm. in diameter and 8 cm. apart. Cell C was 8 cm. longer than cell B, and the electrodes were 8 cm. further apart; the cells were otherwise identical. Cell D was designed according to Jones and Bollinger.¹⁰ The electrodes were unplatinized and their area and the distance between them were approximately the same as for cell A.

An oil thermostat controlled the temperature to 0.01°.

TABLE I

RATE OF CHANGE OF CONDUCTIVITY OF SODIUM HYDROXIDE SOLUTIONS DUE TO SOLUTION OF GLASS

Cell	Alkali concn., N	Change in % per hr., at 30°	at 35°
A	0.002	0.022	
B	.005	.064	
B	.008		0.10
B	.030	.022	
C	.015	.030	.050
C	.050	.012	

Materials.—Tertiary butyl acetate was prepared according to Skrabal and Hugetz,¹¹ oxamide according to Liebig¹² and oxamic acid according to Oelkers.¹³ Dimethylglycine was synthesized by the method of Michaelis and Schubert¹⁴ and the chloride of betaine amide by the method of Renshaw and Hotchkiss.¹⁵ To determine its purity, each was analyzed before use.

Tertiary Butyl Chloroacetate.—While the tertiary butyl chloroacetate used in the velocity determinations was prepared by direct esterification, a more convenient method of preparation follows: 60 cc. of chloroacetyl chloride was placed in a three-necked flask equipped with thermometer, stirrer, dropping funnel and an outlet protected by a calcium chloride tube. A mixture of 100 cc. of dimethylaniline and 75 cc. of tertiary butyl alcohol (m. p. 23°) was added dropwise during the course of an hour, maintaining the temperature at 0° by means of an ice-bath. At the end of this time, the ice-bath was removed and the mixture allowed to stand overnight. Water was then added, and the heavy ester layer separated, washed with water, dilute hydrochloric acid, sodium bicarbonate solution, and water again. The oil was dried over calcium chloride and vacuum distilled: yield, 72 g., or 60%, of the ester. The product is a colorless liquid, slightly heavier than water, boiling at atmospheric pressure at 155° with some decomposition and at 60.2° at 15 mm., n_D^{20} 1.4230.

Anal. Calcd. for $C_6H_{11}O_2Cl$: C, 47.8; H, 7.37; Cl, 23.56; sapon. equiv., 150.5. Found: C, 47.6; H, 7.33; Cl, 23.63; sapon. equiv., 150.6.

The material actually used in the velocity determinations had been carefully fractionated at reduced pressure, and was of analytical purity.

An acidified portion of completely saponified ester gave no precipitate with silver nitrate, showing that there is no appreciable hydrolysis of the chlorine during saponification. Another portion of the ester was hydrolyzed, the

tertiary butyl alcohol isolated, dried, and identified by melting point and the melting point of a mixture with an authentic sample.

Tertiary Butyl Betainium Chloride.—Twenty grams of tertiary butyl chloroacetate and 62 cc. of a 2.5 molar solution of trimethylamine in dry benzene were mixed with cooling. Although crystals formed in a few minutes, it proved advisable to allow the mixture to stand for twenty-four hours; yield, 18 g. The crude material can be crystallized from acetone or dioxane to which a small amount of water has been added. The product is a white crystalline powder, which, when dry, melts with decomposition around 220°, the exact temperature depending somewhat on the rate of heating.

Anal. Calcd. for $C_8H_{20}O_2NCl$: Cl, 16.91; N, 6.68. Found: Cl, 16.89; N, 6.79.

The material used in the rate determinations had been recrystallized several times, and was of analytical purity.

Tertiary Butyl Dimethylglycinate.—Twenty grams of tertiary butyl chloroacetate and 43 cc. of a 4 molar solution of dimethylamine in dry benzene were mixed, with cooling, and allowed to stand at room temperature for twenty-four hours. The resultant material was extracted with 1:1 hydrochloric acid, and the extract washed once with ether. The aqueous layer was then saturated with potassium carbonate and extracted with ether. The ether extract was dried with potassium carbonate, the ether removed by distillation, and the residue fractionated at reduced pressure. The yield of colorless oil, having a slight ammoniacal odor, was 12 g. The hydrochloride was prepared by adding a slight excess of hydrogen chloride in methanol, and evaporating to dryness under reduced pressure. The residue can be recrystallized from a 10% solution of tertiary butyl alcohol in benzene. The white twice recrystallized material which was used in the velocity determinations melted about 150°, the exact temperature depending somewhat on the rate of heating.

Anal. Calcd. for $C_8H_{18}O_2NCl$: Cl, 18.13; N, 7.16. Found: Cl, 18.08; N, 7.12.

Conductivity water and carbonate free alkali were used throughout. Chemicals other than those recorded here were of reagent grade.

Method.—The usual procedure in the determination of reaction velocity by conductivity is to determine the initial and final conductivities of the solution and to calculate the rate on the assumption that the conductivity of the solution is a linear function of the extent of reaction. In the determinations here described, since it was inconvenient in most cases to measure the initial and final conductivity, each velocity determination was standardized by measuring the conductivity of solutions corresponding in ionic composition to that present at several different times during the reaction.¹⁶ Since the concentrations of the various ions in the standardizing-solution could not conveniently be made exact

(16) A similar standardization procedure has been described by Crocker and Lowe, *J. Chem. Soc.*, 91, 952 (1907).

(10) Jones and Bollinger, *J. Am. Chem. Soc.*, **53**, 411 (1931).

(11) Skrabal and Hugetz, *Monatsh.*, **47**, 17 (1926).

(12) Liebig, *Ann.*, **9**, 1 (1834); see "Beilstein," IV ed., Vol. II, p. 546.

(13) Oelkers, *Ber.*, **22**, 1566 (1889).

(14) Michaelis and Schubert, *J. Biol. Chem.*, **115**, 221 (1938).

(15) Renshaw and Hotchkiss, *J. Am. Chem. Soc.*, **48**, 2698 (1926).

duplicates of those at any point during the reaction, a small correction had to be added to the conductivity of each standardizing solution. In order to estimate this correction, it was only necessary to know the ratios of the conductivities of all the ions present to that of hydroxide ion.

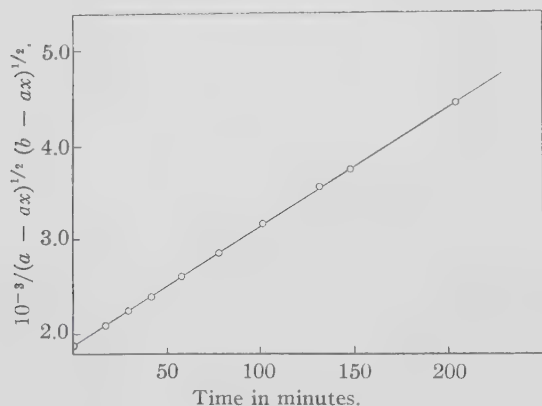


Fig. 1.

The values of the conductances are given in Table II, arbitrarily assigning to hydroxide ion a value of 100 at every temperature. The values in the upper part of the table were calculated from existing data,¹⁷ those in the lower part of the table were measured. Since the correction was in all cases small, comparatively large errors in the relative conductivities of the ions do not affect the final result appreciably. The measurements were made in an ionic environment similar to that in the actual reaction mixtures, except in the case of tertiary butyl betainium chloride, which was measured in a solution containing only the pure compound.

TABLE II
RELATIVE CONDUCTIVITIES OF THE IONS

Ion	Temperature		
	6.5°	10°	30°
Hydroxide	100.0	100.0	100.0
Chloride	39.0	38.7	
Acetate	20.6		
Oxalate			70.3
Sodium	24.7	24.7	24.7
Ammonium			35.6
Chloroacetate	16.6		
Oxamate			18.7
Dimethylglycinate	12.5		
Betaine amide	19.8		
<i>t</i> -Butylbetainium	17.8		

In some cases there was a slow reaction between the ions of the standardizing solutions. Since

(17) Landolt-Börnstein, "Physikalisch-chemische Tabellen," Erg. IIIc.

the extent of the reaction was always quite small, it was not difficult to extrapolate accurately back to the time when the solution was prepared. The procedure could not be used for tertiary butyl betainium chloride, because of the rapid reaction of the positive ion with alkali; therefore the corresponding amide was used in place of the ester. After determining the relative conductivities of the ester and amide ions, it was possible to estimate the conductivities of the solutions used in the reaction velocity determinations. While the error in this case is probably greater than in any other, it cannot be large, since only 10% of the total conductivity is contributed by the positive ion.

Results

The data for a typical velocity determination, the saponification of tertiary butyl chloroacetate, are given in Table III. Here a is the initial concentration of sodium hydroxide in moles per liter, b the initial concentration of the ester, and x the fraction of the alkali consumed in time, t . The rate constants were obtained graphically by plotting time against $\log(1 - x)/(b - ax)$, or, when the initial concentrations of the two reactants were nearly equal, against $1/(a - ax)^{1/2}(b - ax)^{1/2}$. Figure 1 is a graph of the data in Table III.

TABLE III
DATA FOR THE SAPONIFICATION OF TERTIARY BUTYL
CHLOROACETATE

$a = 0.000782$ Time in min.	$b = 0.000835$ Conductivity	x
0.0	4462	0.346
17.4	4165	.420
29.1	4000	.461
41.4	3851	.498
57.3	3683	.540
77.3	3510	.583
101.2	3334	.627
131.6	3170	.667
147.7	3094	.686
203.8	2887	.738
262.9	2727	.778

Conductivity in this case is a linear function of the extent of reaction. When $x = 0.010$ the conductivity is 5813 and when $x = 0.660$ the conductivity is 3197. The conductivities are all in arbitrary units.

The solution of glass in alkali changes both the conductivity and the hydroxide-ion concentration. In correcting for the former effect, it was assumed that the percentage time rate of change of conductivity due to reaction with the

TABLE IV
SUMMARY OF THE VELOCITY DETERMINATIONS

Organic reactant	Cell	a	b	μ	T	k in min. ⁻¹ (mols/l.) ⁻¹
Oxamide	B	0.004669	0.003207	0.00467	30.1°	1.36
	A	.002076	.001301	.00208		1.40
						Av. 1.38
Sodium oxamate	C	.05504	.05492	.110	30.1°	0.0158
	B	.03209	.02676	.0589		.0143
	B	.02732	.01738	.0447		.0138
	C	.01424	.01197	.0262		.0132
				Value for infinite dilution		.0101
<i>t</i> -Butyl dimethylglycinate	B	.01408	.01618	.0303	10.2°	.0220
	B	.00731	.00866	.0160		.0228
						Av. .0224
<i>t</i> -Butyl betainium chloride	D	.002143	.002112	.00426	10.2°	23.5
	D	.000849	.00776	.00163		23.8
	D	.000841	.00835	.00168		21.0
	A	.000596	.000593	.00119		(18.9)
	D	.0005042	.0004880	.000992		20.7
	A	.0005042	.0004880	.000992		20.8
	D	.0004354	.0004288	.000864		23.2
						Av. 22.2
<i>t</i> -Butyl acetate	B	.03181	.01981	.0318	6.6°	0.0247
	B	.01421	.04087	.0142		.0254
	A	.002269	.01421	.00227		.0244
						Av. .0248
<i>t</i> -Butyl chloroacetate	D	.000782	.000835	.000782	6.6°	11.9
	A	.000629	.000587	.000629		(14.4)
	D	.000582	.000570	.000582		21.1
	A	.000582	.000570	.000582		12.5
	D	.0004362	.0004405	.000436		12.4
						Av. 12.2

glass is constant during a given experiment. In correcting the latter, the hydroxide-ion concentration at each point was reduced by a factor of $1 - pt$, where p is the percentage time rate of change of hydroxide ion and t the time. It was assumed that the change in hydroxide-ion concentration was 1.6 times the change in conductivity given in Table I. While neither of these computations is exact, the total correction is so small that the methods used will cause no serious errors.

In the case of the saponification of the ester of dimethylglycine, the base formed, dimethylglycinate ion, contributes to the hydroxide-ion concentration. So does the ammonia formed in the hydrolysis of sodium oxamate and of oxamide. Furthermore, in this latter case, the hydrolysis of the second amide group will be a complicating factor. However, these corrections are so small that the values of the velocity constants obtained using a standard bimolecular form are not significantly different from those obtained by more complicated equations in which these corrections are,

at least to a first approximation, embodied.¹⁸

The constants for all the velocity determinations are collected in Table IV. Here μ is the initial ionic strength, k the rate constants in inverse minutes and inverse moles per liter. The initial concentrations were varied at least two-fold; the constants usually deviate less than 5% from the average. The values in parentheses were not used in averaging.

The observed rate constants for the hydrolysis of sodium oxamate increase with increasing ionic

(18) For the hydrolysis of sodium oxamate and the tertiary butyl ester of dimethylglycine, for example, the following equation takes into account the ionization of the base.

$$kt + C = \frac{1}{[a(a-b)^2 + a^2K_B]} \left\{ -a(a-b+K_B) \log_e(b-ax) + \frac{a(a-b+K_B)}{2} \log_e[a(1-x)^2 + K_B] + b\sqrt{aK_B} \tan^{-1} \frac{ax-a}{\sqrt{aK_B}} \right\}$$

Here a is the initial concentration of sodium hydroxide, b that of the ester, k is the rate constant, K_B the ionization constant of the base, and x the fraction of the sodium hydroxide that has been consumed at time, t . C is a constant of integration. When the second stage hydrolysis of oxamide is taken into account, the equation is even more complex.

strength. Since the reaction is one between two negative ions, Brönsted's theory⁷ predicts a positive primary salt effect. However, at the ionic strengths at which the measurements were made, the observed salt effect is less than the theory predicts. Extrapolation of the plot of $\log k_{\text{obsd.}}$ against the square root of the ionic strength gives a value of 0.0111 for the rate constant; extrapolation of the lowest point using the theoretical limiting slope gives a value of 0.0091. These are an upper and lower value, respectively, for the true value at infinite dilution. For the purposes of the present paper, the mean value, 0.0101, is sufficiently precise. Since the saponification of tertiary butyl betainium chloride was carried out at very low ionic strength, and since the accuracy of these measurements is not very great, extrapolation to infinite dilution does not seem warranted.

The ion $(\text{CH}_3)_2\text{N}^+\text{HCH}_2\text{CO}_2\text{C}(\text{CH}_3)_3$ would be expected to saponify at a rate several hundred times greater than that of the free base. However, an estimate of the base strength of the ester (from the base strength of glycine ethyl ester¹⁹) indicates that, in solutions of the alkalinity employed in the velocity determinations, no significant part of the rate can be due to hydrolysis of this ion.

The logarithms of the ratios of the rates, corrected for statistical factor, for substituted and unsubstituted compounds ($\Delta \log k$) are assembled in Table V. It is at once obvious that errors of the magnitude indicated for the velocity constants will have no significant effect upon these logarithms.

Discussion of Results

From the data given in Table V and Kirkwood's and Westheimer's equations, it is possible to compute the separation of the polar substituent and the negative charge contributed by the

TABLE V
SEPARATION OF CHARGE AND SUBSTITUENT, COMPUTED FROM VELOCITY DATA

Organic reactants	$\Delta \log k$	Separation in Å.		
		R	R_D	R_B
Oxamide	1.84	4.15	3.85	1.71
Sodium oxamate				
<i>t</i> -Butyl betainium chloride	3.02	4.85	4.05	1.02
<i>t</i> -Butyl ester of dimethylglycine			(glycine) 4.25 (betaine)	
<i>t</i> -Butyl chloroacetate	2.70	3.15	3.00	0.48
<i>t</i> -Butyl acetate				

(19) Edsall and Blanchard, *J. Am. Chem. Soc.*, **55**, 2337 (1933).

hydroxide ion to the activated complex. In order to carry out these calculations, the volumes of the molecules have been estimated, as usual, by using Traube's rule.²⁰

The computations for oxamide were made on the basis of a spherical model, with the charges on a diameter. The distance between a positive charge placed approximately as the proton in oxamic acid, and the negative charge of the activated complex, is given to the nearest 0.05 Å. by R ; it is compared with R_D , the separation of the protons in oxalic acid computed in a similar manner from dissociation constant measurements.

The calculations for tertiary butyl chloroacetate are more complicated. The difference between the carbon-chlorine dipole moment and the carbon-hydrogen moment was taken as 1.86 Debye units.²¹ The negative charge of the activated complex was placed arbitrarily on the extension of that carbon to carbon bond nearest the ester linkage in the acid portion of the molecule. The computations were made on the basis of two different assumptions. First, the charge and dipole were placed equidistant from the center on a diameter, and, second, the charge was placed at the center of the molecule.²² The two methods led to values of R differing by 0.4 Å.; the average is given in Table V. The value of R_D is that obtained from computations based on the ratio of the ionizations constants of chloroacetic and acetic acids.

The computations for the chloride of the tertiary butyl ester of betaine were made both on the basis of an ellipsoid with the charges at the foci, and on the basis of a sphere, with the charges on a diameter, but the positive charge twice as far from the center of the sphere as the negative charge.²³ Again the two methods give values

(20) Traube, *Saml. Chem. Chem.-tech. Vortr.*, **4**, 255 (1899).

(21) Smyth, *J. Phys. Chem.*, **41**, 209 (1937).

(22) In this case, the equation for the electrostatic work reduces to the form

$$\Delta \log k = \frac{eM \cos \zeta}{2.303 k' TR^2 D_1}$$

where e is the electronic charge, M the dipole moment of the substituent, ζ the angle between the dipole and the line joining it to the center. D_1 the "internal dielectric constant," has been assigned the value of 2.00, as previously.

(23) In this case the appropriate value of the "effective dielectric constant" is given by the equation

$$1/D_E = \frac{1}{D_1} \left[1 - \frac{x_1 + x_2}{1 + x_1 x_2} \right] + \frac{1}{D} \left[\frac{2(x_1 + x_2)}{1 + x_1 x_2} - \frac{x_1 + x_2}{x_1 x_2} \log_e (1 + x_1 x_2) \right]$$

where $x_1 = r_1/b$ and $x_2 = r_2/b$. r_1 and r_2 are the distances of the first and second charges from the center, b the radius of the sphere.

differing by about 0.3 Å.; the average appears in the table.

There is no value of R_D obtained from ionization constant data which is strictly comparable with this value of R . For, while the ionization constant of betainium chloride is known, the ionization constant of dimethylglycine, due to its zwitterionic structure, cannot be considered that of the corresponding unsubstituted acid. However, the strength of betainium chloride was compared with that of trimethylacetic acid,¹⁷ the "isosteric" structure,²⁴ in which a carbon atom rather than a nitrogen atom holds the three methyl groups. Neuberger's data show that this is a fair approximation.²⁵ The length given in Table V is the average of one in which the molecule is regarded as an ellipsoid with charges at the foci, and one in which the molecule is regarded as a sphere with the charges equidistant from the center on radii separated by the tetrahedral angle. Fortunately, these two values of R_D differ by only 0.3 Å. The value of R_D for glycine is placed alongside the approximate one for betaine.

The values of R_B were computed using Bjerrum's² and Eucken's⁴ equations. In the case of the chloroester, the fully extended model was used in determining the value of R_B .

Inspection of Table V reveals that, despite the approximations made in assigning simple shapes to these esters and amides, the values of R obtained from velocity data are in good agreement with R_D , computed from dissociation constants.

(24) Schwarzenbach, *Z. physik. Chem.*, **A176**, 133 (1936).

(25) Neuberger, *Proc. Roy. Soc. (London)*, **A158**, 68 (1937).

It must be stressed that these latter values have previously been shown in all cases to be of reasonable magnitude. The values of R_B , obtained from the Bjerrum equation, are, however, much too small. Since R appears as the square in the equation for the potential of a dipole, the inadequacy of the simple equation in the case of the chloroester, serious as it appears, is actually even more significant.

The retardation caused by a negative charge, the acceleration caused by a positive charge and a dipole in saponification, are not only qualitatively but quantitatively in accord with predictions made on the basis of the electrostatic effect of the substituents.

Summary

1. The electrostatic theory has been applied to the problem of the effect of polar substituents on reaction velocities.

2. The rates of alkaline hydrolysis of the following pairs of compounds have been measured: oxamide and sodium oxamate, tertiary butyl acetate and tertiary butyl chloroacetate, the tertiary butyl ester of dimethylglycine and the chloride of the tertiary butyl ester of betaine.

3. By means of the equations previously developed by Kirkwood and Westheimer, it has been shown that the ratio of the rates for each pair is quantitatively in accord with the hypothesis that the effect of a polar substituent on the velocity of these hydrolyses is primarily electrostatic in origin.

